GENERAL REVIEW AND ENFORCEMENT POLICIES

PROCEDURES FOR PROCESSING DRUG EXPERIENCE REPORTS

I. Purpose:

This guide establishes procedures for handling drug experience and adverse reaction reports.

II. Document Control Unit Procedures:

A. DCU stamps all drug experience reports (DERs) received, prepares a list recording the date of the letter, the date it is received, and the name of the firm.

B. The reports are then forwarded to the Division of Epidemiology and Surveillance.

III. Drug Experience Reports:

A. If a DER is received directly by the Division of Epidemiology and Surveillance (HFV-210), it is forwarded to DCU for processing according to the procedures listed in paragraph 2.

B. A DER is categorized according to report type and information contained in the submission using DER System Codes. Categories under the system correspond to records and reports information required by 21 CFR 510.300 and 301.

1. Report types:

a. Code A - Special
b. Code B - Regular Six Month
c. Code C - Regular Annual

2. Submission types:

a. Code A - Up-to-date Report with Supplement
b. Code B - Promotional material only
c. Code C - without Adverse Reactions
d. Code D - With Adverse Reactions from Firm

e. Code E - With Adverse Reactions not from Firm
f. Code F - Letter Only (Other than Adverse Reactions)
g. Code G - Other
h. Code H - Information Previously Requested
i. Code I - Progress Report on Adverse Reactions
j. Code J - Product not Marketed/Manufactured
k. Code K - Manufacturer's Complaint

C. Information not reported as DER:

1. Information required under 21 CFR 510.300 and 301 but not received as a DER (telephone report of an adverse drug reaction, etc.) will be identified with the appropriate NADA number and forwarded to DCU.

2. DCU will code the information as a DER and forward to the Division of Epidemiology and Surveillance for processing.

IV. Supplement with 510.300 Reports:

A. An NADA supplement containing a 21 CFR 510.300 report is logged in by DCU and acknowledged by date stamping the cover page.

B. It is coded as a supplement NADA with an accompanying DER and this information is entered into the Center's STARS database.

C. The supplement is then sent to the appropriate division together with the respective NADA file.

1. If regulatory supplements are received by a New Animal Drug Evaluation Division or voluntary supplements are received by the Division of Epidemiology and Surveillance, the receiving unit should immediately route the supplements to DCU with an explanation.

2. DCU will forward the supplements to the appropriate division.

D. DERs submitted with a supplement should immediately be referred to the Division of Epidemiology and Surveillance if they include information on adverse reactions, or information that reflects on the safety and/or efficacy of the drug. These reports will be given priority review.

1. If no action is indicated for the reports, the Division of Epidemiology and Surveillance will immediately advise the appropriate Division so that processing of the supplements will not be delayed.

2. If the reports do not contain information on adverse reactions, safety, and/or efficacy of the drug, they may be forwarded to the DCU for separation or duplication and recoding and then forwarded to the Division of Epidemiology and Surveillance.

3. If the firm makes a statement in the supplemental application such as, "There are no required 21 CFR 510.300 reports to be submitted as this time," then New Animal Drug Evaluation personnel can, after verifying with the Division of Epidemiology and Surveillance, regard this statement as meeting the requirements of 21 CFR 514.8(a)(1) regarding submission of reports with a supplemental application.

E. Some Category II supplements under 21 CFR 514.106(b)(2) may require a re-evaluation of the safety and effectiveness data in the parent application. Therefore, for these supplements, approval may be delayed or even withheld if an assessment of the current status of DERs and the information they contain, indicates such an action is warranted.

1. To expedite this determination, the Division of Epidemiology and Surveillance will make its files available to New Animal Drug Evaluation personnel to allow them to determine for themselves the status of DERs. The New Animal Drug Evaluation reviewer should request assistance from the appropriate Division of Epidemiology and Surveillance Team Leader (or other professional personnel) if unfamiliar with the Division of Epidemiology and Surveillance file system.

2. If the DER files contain sufficient evidence to question the advisability of approving the supplement or if the Division of Epidemiology and Surveillance already has an action pending against the NADA, the appropriate Team Leader in the Division of Epidemiology and Surveillance should be contacted to coordinate activities on the NADA.

3. Once the review of the marketing history of the product is completed, it should be summarized or referenced directly in the technical review of the supplement.

   a. If the information does not adversely affect approval of the supplement this should be specifically stated by the New Animal Drug Evaluation reviewer. The following statement is considered appropriate:

      "DER summaries in the Division of Epidemiology and Surveillance

were reviewed and do not provide an adequate basis for refusal to approve this supplement."

b. If the information is such that significant questions are raised and resolution must be made, the following statement is considered appropriate:

"DER summaries in the Division of Epidemiology and Surveillance were reviewed and raised significant questions concerning the effect the proposed change will have on the safety of this product. The firm should be requested to resolve this issue prior to approval of the supplement."

4. Reviewers in the Division of Epidemiology and Surveillance will inform the appropriate New Animal Drug Evaluation Team of serious problems with approved products when they arise. Determination of the significance of these problems relative to supplemental NADA approval will be in accordance with the procedures described above.

5. Division of Epidemiology and Surveillance will send the Office Director for New Animal Drug Evaluation a copy of each letter they issue to the sponsor pertaining to an approved drug.

V. DER Abstraction:

A. Upon completion of coding, the DER is assigned to a reviewer within the Division of Epidemiology and Surveillance who abstracts information according to the content of the report.

1. DER abstracts are recorded. The records are then filed by NADA number within the Division of Epidemiology and Surveillance.

2. Adverse reaction reports, submitted as part of the DER, are filed by NADA number within the Division of Epidemiology and Surveillance.

3. The ADR reports are reviewed, coded, and entered into the Division's ADR database.

B. When action is indicated, the DER is returned to the Team Leader by the reviewer for concurrence. The action is issued by the Division of Epidemiology and Surveillance prior to returning the DER to the files.

C. Continuing stability studies are reviewed by the chemists in the Division of

Manufacturing Technologies.

D. If it is determined that a supplement or amendment is presently under consideration an extra copy of the abstract is forwarded to the processing Division. All adverse reactions listed for the NADA of the supplement submitted will be available in the Division of Epidemiology and Surveillance.

E. There are no report requirements on Master Files or Food Additive Petitions. Manufacturers of finished feeds are exempt from routine reports requirements of 21 CFR 510.300(b)(4)(ii) but are not exempt from the requirements of 21 CFR 510.300(b)(1) and (2) (which are specifically covered under 21 CFR 510.301).

F. All correspondence requiring a reply is placed in a pending file. This file is reviewed on a biweekly or monthly basis and any necessary follow up is made.

G. When a master file becomes an NADA, the date of approval of the NADA is the anniversary date for reporting DERs.